



EVALI: E-Cigarette or Vaping-Associated Lung Injury

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Managed Care APPE Rotation
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Objectives



Define EVALI



Epidemiology



Recognize key signs and symptoms



Discuss diagnosis and management



Familiarize with key updates and how to prevent EVALI

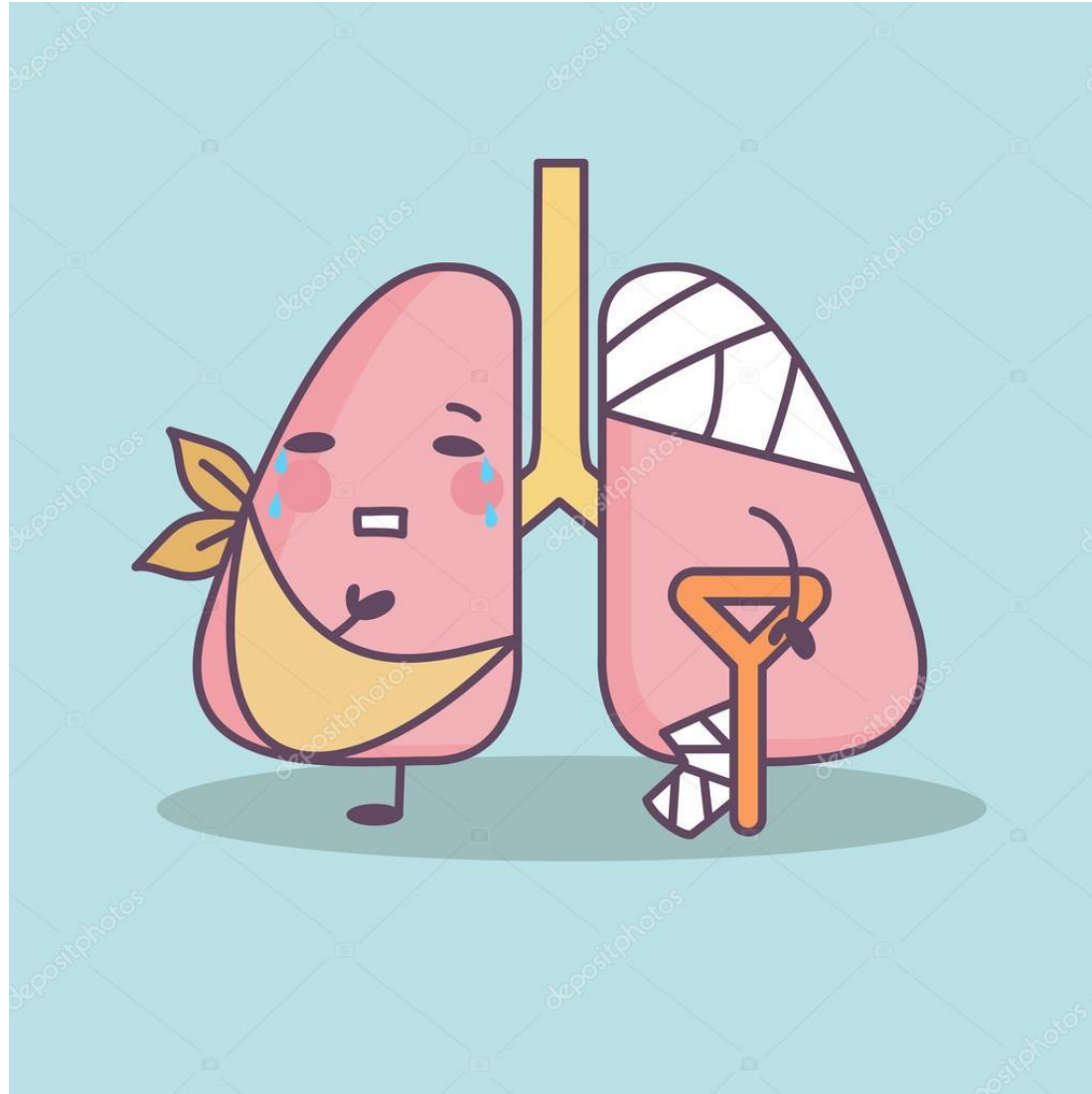
Background





What is EVALI?

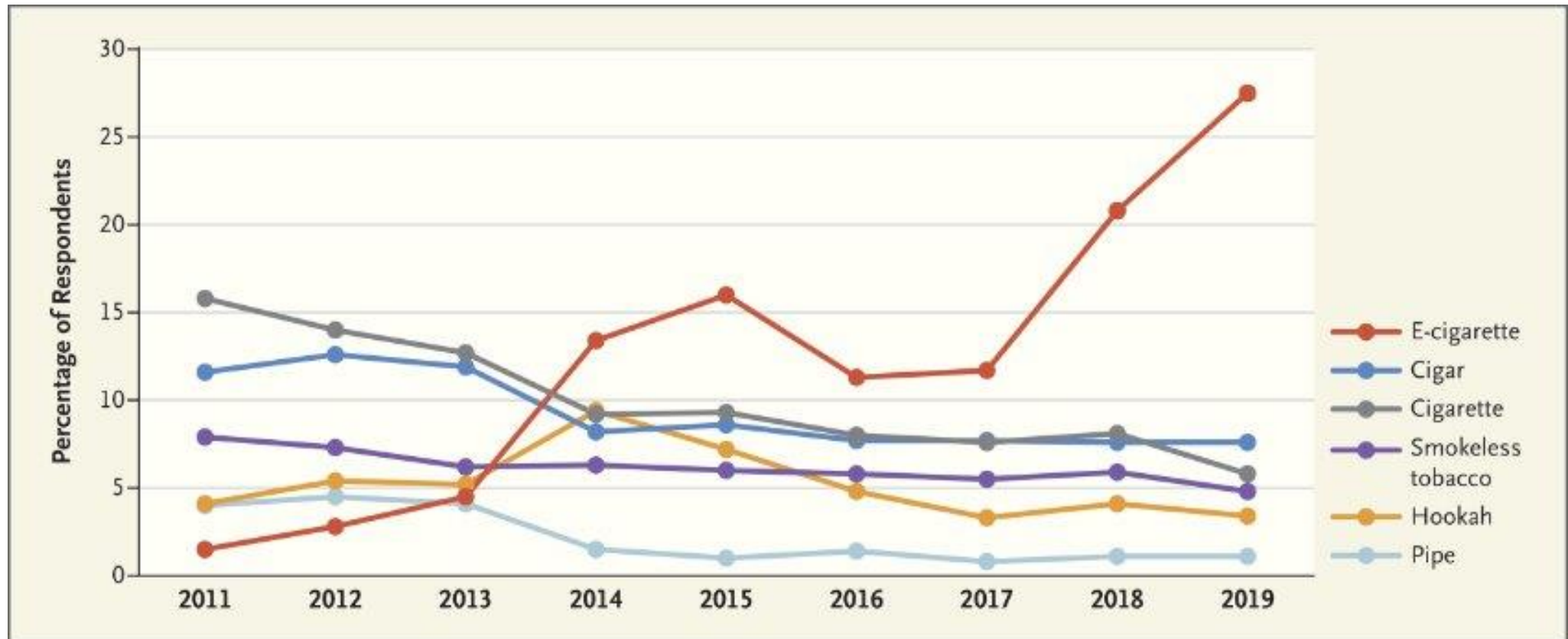
- EVALI: E-cigarette or Vaping-Associated Lung Injury
- Identified in 2019 following a cluster of cases linked to the use of e-cigarettes and vaping products (CDC)
- Characterized by lung inflammation



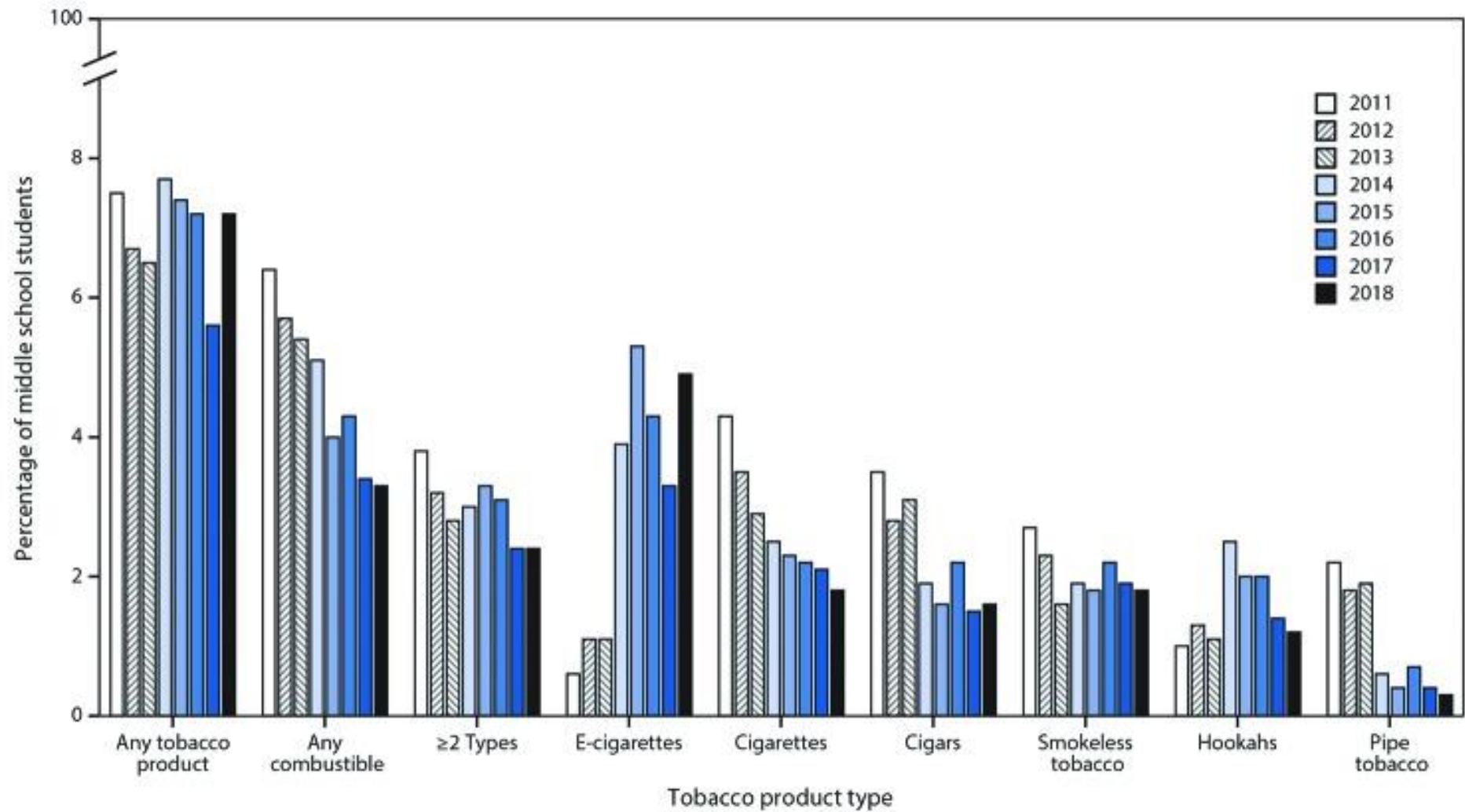
Epidemiology



- Over 2,800 cases and 68 deaths reported in the U.S
- Predominately affects adolescent and young adults



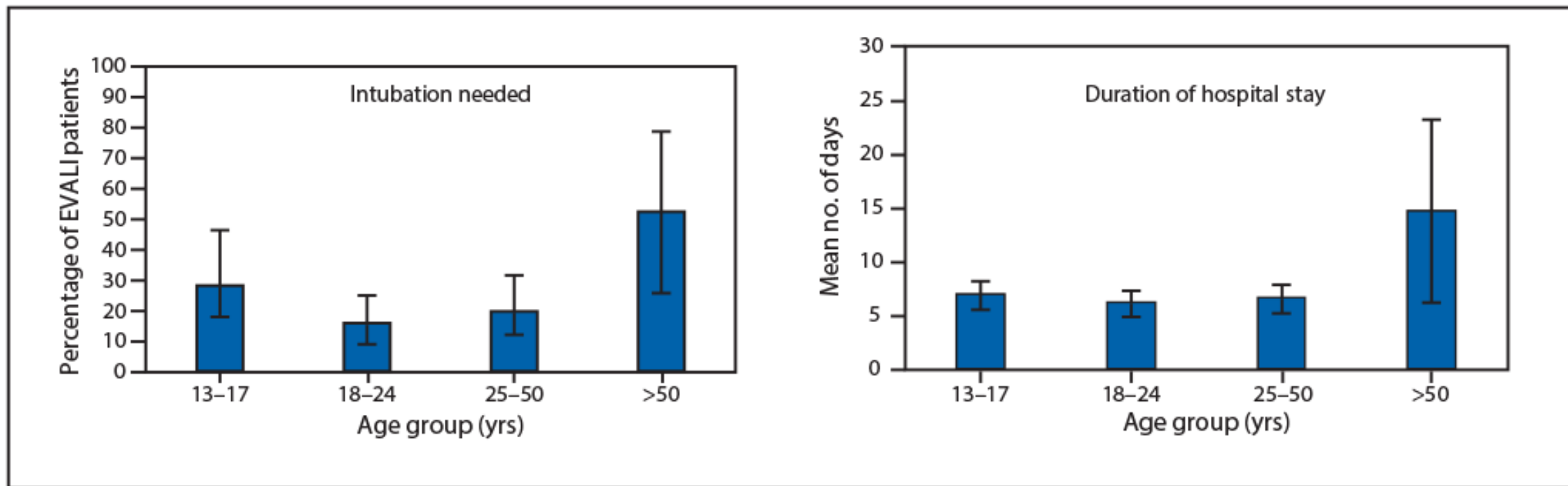
Case Trends



CDC 2019 Statistics



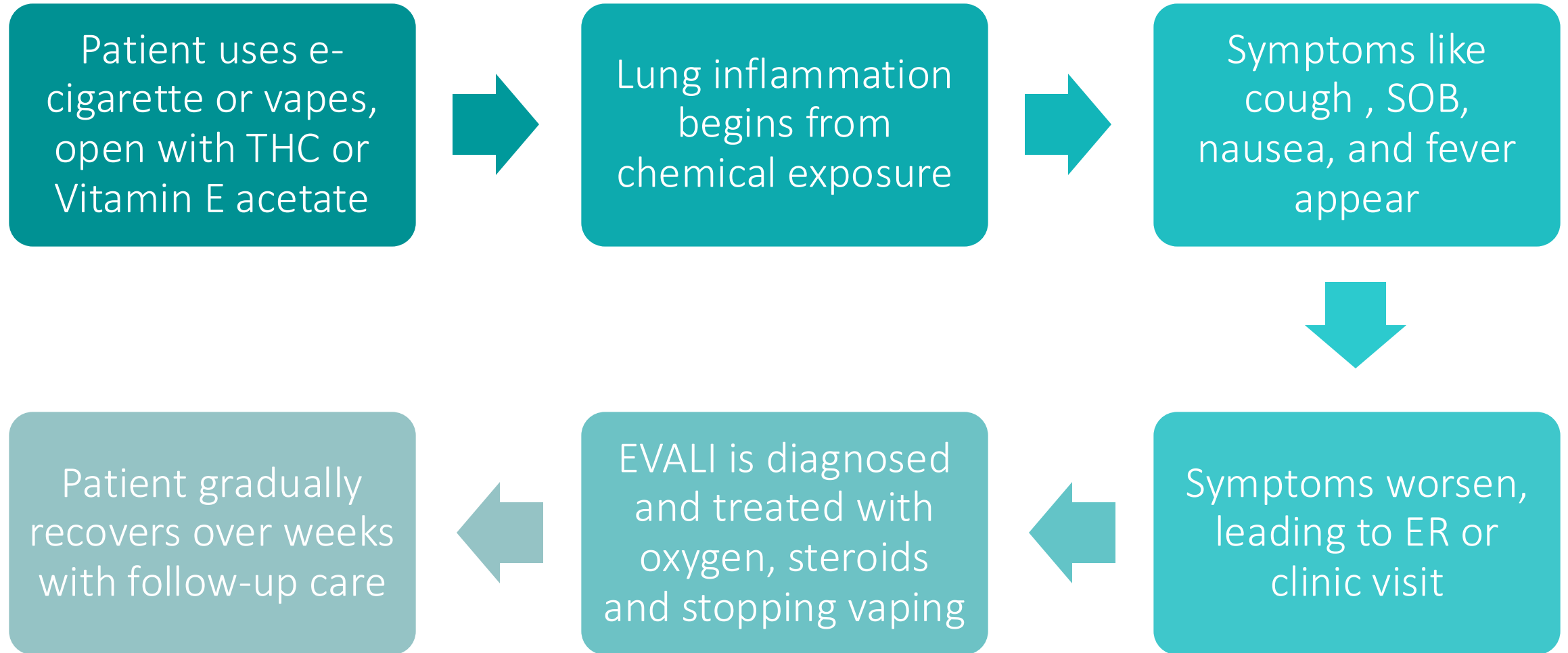
CDC 2019 EVALI Statistics:



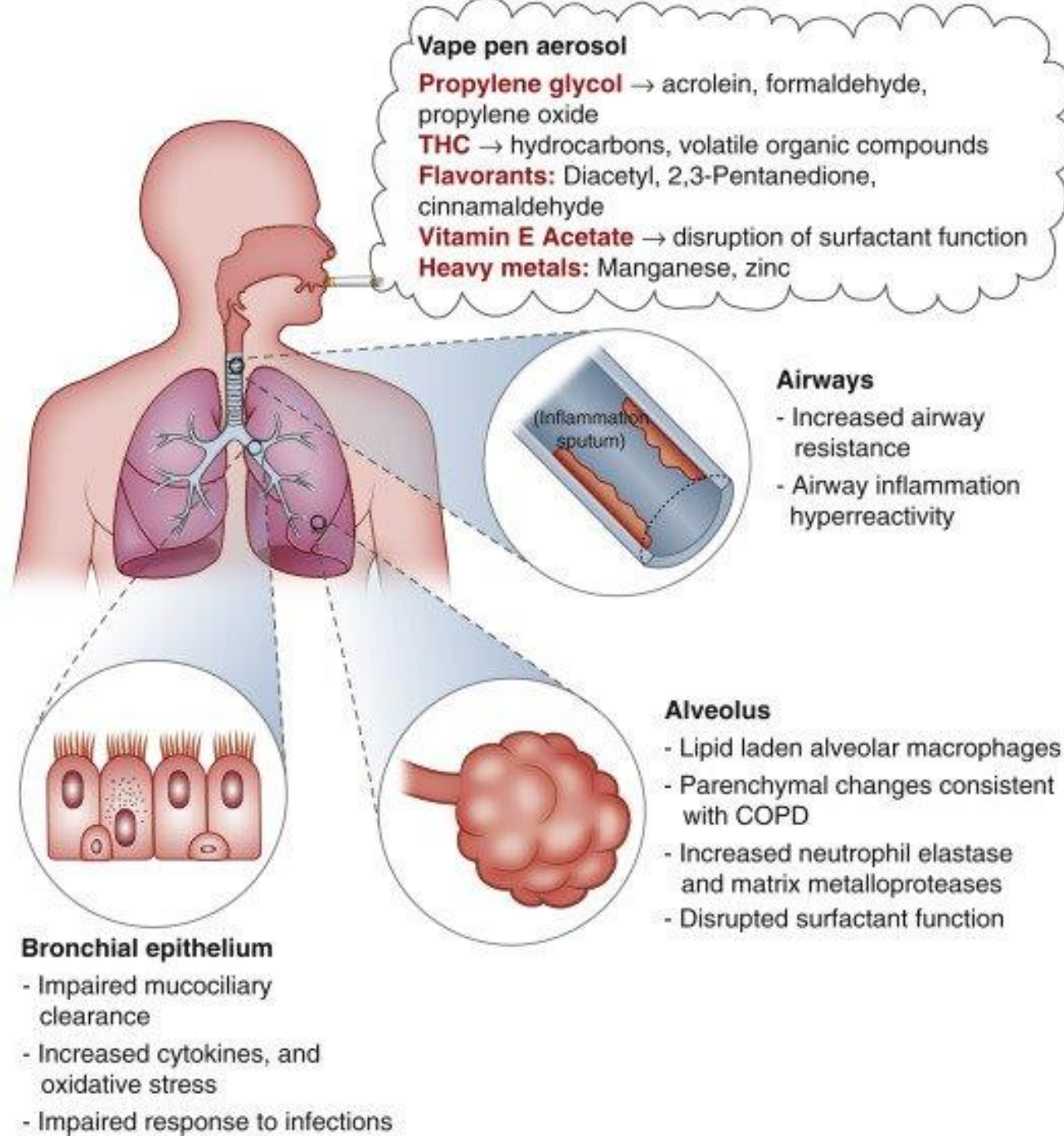
Percentage of persons needing intubation (N = 338) and hospitalization (N = 242) among patients with e-cigarette, or vaping, product use associated lung injury (EVALI), by age of patient — United States, February 1–October 3, 2019*



Development of EVALI



Pathophysiology



How vaping works?

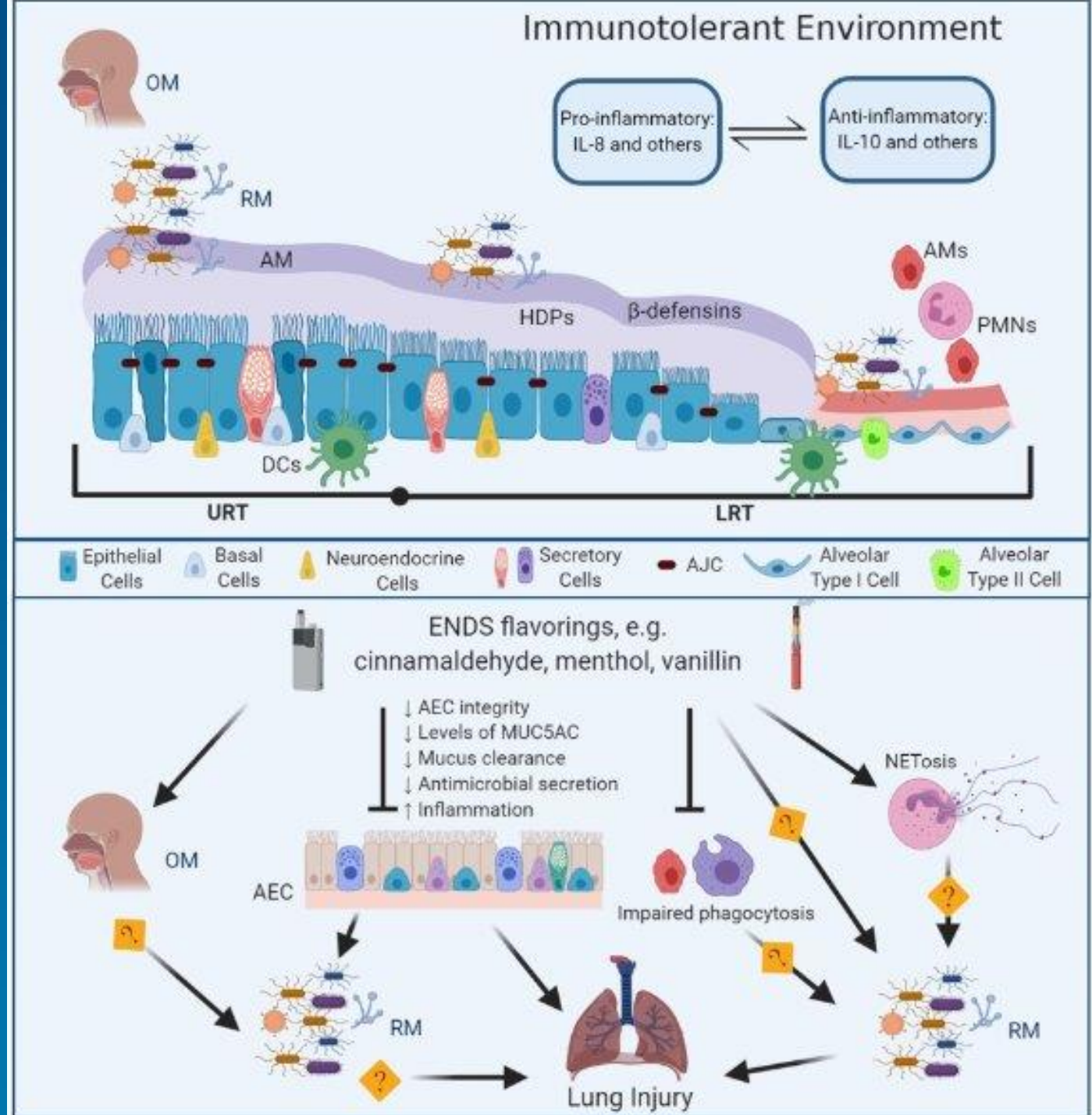
- Direct chemical injury happens from inhaled toxins causing disrupted lung surfactant and cell integrity
- Alveolar permeability
- Fluid, proteins and immune cells leak into alveoli
- May trigger cytokine release IL-6, IL-8, TNF-alpha, worsening the inflammation
- Can mimic or progress to ARDS (Acute Respiratory Distress Syndrome)



Lipid-Laden Macrophages:

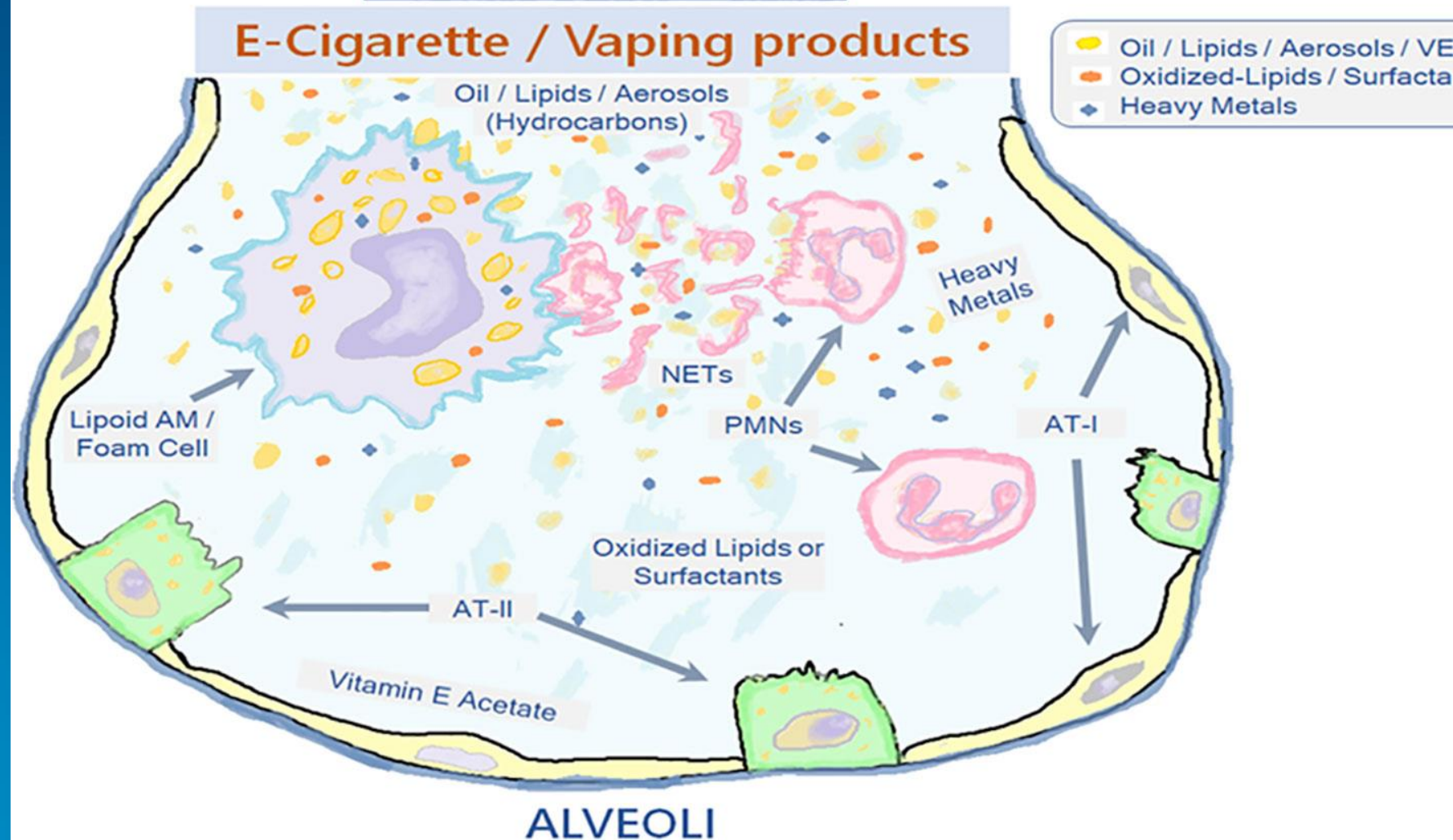
- Vitamin E acetate and oils are poorly cleared by the lung
- Macrophages engulf these lipids, forming "foamy" macrophages
- These are key markers in bronchoalveolar lavage fluid (BAL)
- May contribute to oxidative stress and impaired microphage function

Mechanism of e-liquid flavorings



Pathophysiology

THC containing
counterfeit
ENDS cartridges



Immune Response Shift

- EVALI

- High neutrophil counts CD163 (-) M1 macrophages - pro-inflammatory
- Increase in inflammatory markers:
 - IL-6, IL-8
 - TNF- α
 - CCL2
 - Serum Amyloid A



What are IL and TNF markers and how do they work?

- IL-6: Interleukin-6 is a pro-inflammatory cytokine
 - Mediates acute phase response
 - Fever
 - Stimulates immune response
 - Produced by T cells, macrophage, other
- IL-8: Interleukin-8 Chemokine CXCL8
 - Attracts neutrophils to sites of infection/inflammation
 - Secreted by macrophages, epithelial cells, airway smooth muscle cells
- TNF-alpha: Tumor Necrosis Factor Alpha
 - Key mediator for systemic inflammation, fever, apoptotic cell death
 - Macrophages, some T cells/mast cells



What are IL and TNF markers and how do they work?

- ELISA (Enzyme-Linked Immunosorbent Assay)
 - Most common for cytokine in blood
- Polymerase Chain Reaction (PCR)
 - Used for mRNA expression of cytokines in tissues
- Flow cytometry
 - Cytokine-producing cells using intracellular staining
- Immunohistochemistry
 - localization
- Multiplex bead assays:
 - detects several cytokines at once



Role in EVALI?

- Elevated IL-6, IL-8, TNF-alpha indicate intense inflammation and immune activation
- It specifically attracts neutrophils to the lungs correlating with neutrophilic alveolitis seen in EVALI cases
- The IL-6 and TNF promote a cytokine storm and alveolar damage
- They recruit inflammatory cells and lead to lung tissue injury
- Amplify immune response -> more damage
- Associated with severe disease and possible hospitalization



Triggers for EVALI?

Vitamin E

- Used as a thickening agent in vape cartridges
- Disrupts lung surfactant
- Triggers inflammatory response

Other additives:

- THC: can be counterfeit cartridges
- MCT: medium chain triglycerides
- Propylene glycol
- Flavorings (toxic when vaporized)



How long does it take to develop EVALI?

- Most cases: few days to a few weeks of frequent use
- First exposure: some cases develop after a few uses of high-risk products (THC cartridges with vitamin E acetate)
- Chronic users: some developed after months or years of regular use
- There is no amount of use that is deemed "safe", risk depends on product content



Timeline for discovery of EVALI



2019

First cluster of lung injury cases reported, CDC investigation is initiated



October 2019

Vitamin E acetate identified as key chemical culprit in lung injury



November 2019

Outbreak peaks: over 2,000 cases and increasing, CDC issues national health alerts



January 21st 2020

2,711 cases of hospitalized EVALI or deaths were reported by all 50 states, District of Columbia, and 2 U.S territories

- 60 deaths had been confirmed



2021-2022

Focus shifted to long-term effects, youth vaping, and lung recover research



2023-2024 -> present

Continued prevention efforts, regulation and small isolated cases, most information has been archived on CDC website



Rise of E-cigarettes and Vapes:

- Early E-cigarettes invented in China (early 2000's)
- Designed as a "smokeless" nicotine delivery system
- Mid-2000's, early brands marketed as safer alternative to smoking



- Large brand name JUUL Labs launches JUUL in 2015 with a sleek USB-like design (appealing to youth, discreet)
- Nicotine salt technology with flavored pods (mango, mint)
- Social media aggressive marketing and influence campaigns, youth friendly imagery and flavors

- E-cigarette use among high schoolers from 1.5% in 2011 to 27% in 2019
- The further restrict FDA flavored pods and advertising
- JUUL removes certain flavors

EVALI

Diagnosis and Symptoms



ICU Admission Criteria

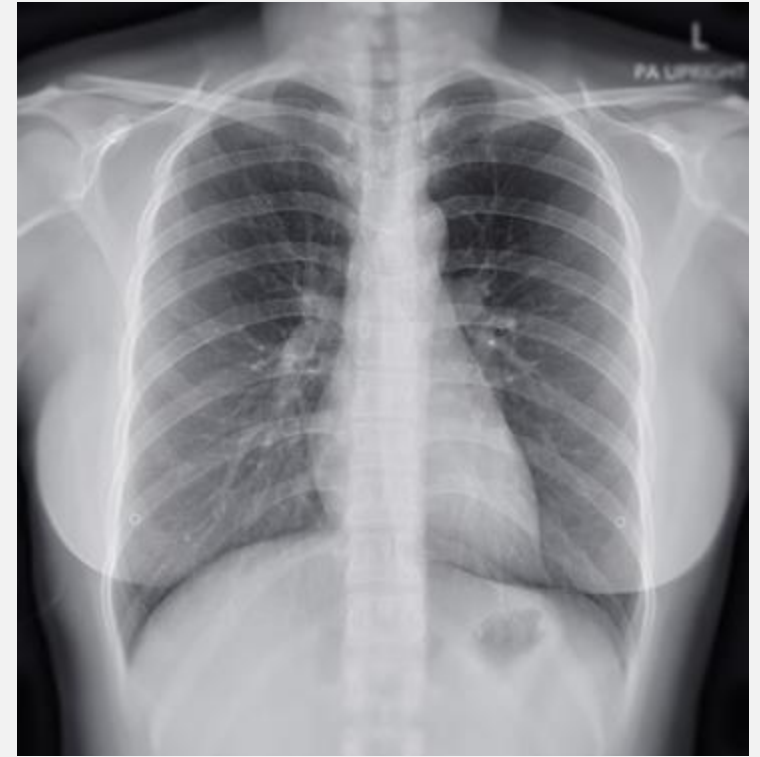


- Severe hypoxia ($\text{SpO}_2 < 90\%$)
- Tachypnea, altered mental status
- Hemodynamic instability
- Multisystem symptoms
(GI + respiratory + fever)



Imaging and Diagnosis

- CT showed ground-glass opacities
pleural effusions
- BAL cytology: lipid-laden macrophages
- Infectious disease workup negative
- Diagnosis: confirmed EVALI per CDC
definition



Clinical Presentation

Cough, shortness of
breath, chest
tightness



Nausea, vomiting,
diarrhea



Fever, fatigue,
malaise



Commonly mimics
pneumonia



CDC Diagnostic Criteria

History of vaping/e-cigarette use within 90 days of symptom onset



Pulmonary infiltrates upon imaging



Negative infectious workup



No more plausible alternative diagnosis



E-Cig Use Associated with Immune Response

- High neutrophil counts, CD163 (+) M2 macrophages - involved in tissue repair, anti- inflammation
- Minimal inflammation - similar to healthy controls



Pharmacologic Interventions

- Systemic corticosteroids (e.g., prednisone or methylprednisolone)
 - IV preferred for hospitalized patients
 - > IV prednisone 60 mg Q6H
 - Oral taper post-discharge
- Empiric antibiotics if bacterial infection can't be excluded
- Supportive medications:
 - Antiemetics
 - Antipyretics
 - Bronchodilators (esp. with asthma history)



EVALI Case Study



Case Study: HG

- 18-year-old male soldier, history of asthma
- Presents with fever, cough, chest pain
- Initial diagnosis: community-acquired pneumonia
- Symptoms worsened despite treatment



EVALI Prevention



Vaping Cessation



- Strong recommendation for cessation of all vaping products
- Education on risks (Vitamin E acetate, THC additives)
 - Behavioral counseling
 - Military tobacco cessation programs
 - Follow-up support



Recovery

- Improvement typically within 4-7 days of steroid therapy
- Some symptoms persistent:
 - Chest discomfort with activity
 - General weakness and fatigue
- Follow-up imaging resolves in around 3 weeks after therapy.



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Prevention Strategies



- Expand access to vaping cessation programs
- Regulate ingredients and labeling in vaping products
- Increase awareness for youth and servicemembers



Unanswered Questions



- Is there genetic susceptibility? Does environment affect EVALI risk?
- Is there a reliable diagnostic biomarker?
- How do you prevent minors from accessing vapes?



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Thank You.

